ISSN 2599-8293

European Commission

CORDIS Results Pack on

the brain

A thematic collection of innovative EU-funded research results

June 2019

How the digital revolution is transforming EU-funded brain research

Research and Innovation

Contents

Editorial

How the digital revolution is transforming EU-funded brain research

As the world continues to be remodelled by the digital revolution, we are seeing digital technologies embed themselves firmly into all aspects of our lives, including into the mainstream of neurosciences research to help unravel the complexity of brain disorders. In this cross-cutting CORDIS Results Pack, we highlight innovative projects from across the full spectrum of EU-funded research programmes that are helping science make sense of arguably the most complex and mysterious machine in existence – the human brain.

Around 165 million Europeans are afflicted with a brain disorder and it is estimated that one in three people will suffer from a neurological and/or psychiatric disorder at some point in their lives. In 2011, the global cost to European healthcare budgets was estimated to be around EUR 800 billion per year and is set to only increase further as Europe's population ages and becomes more susceptible to brain disorders.

Brain disorders come in many forms, from neurodegenerative diseases, with some of the most well-known being Alzheimer's, dementia, schizophrenia and Parkinson's disease. However, other diseases and conditions that are also classed as brain disorders include epilepsy, depression, stroke, migraine, sleep disorders, pain and addiction. Many brain disorders have no cure, such as Alzheimer's and Parkinson's. Others can be managed, but still have wide-ranging effects on the quality of life of patients and their carers.

An EU research priority

Now the research focus on developing new treatment options for patients with brain disorders has taken an inevitable digital turn – harnessing the power of digital technologies and the increasing clout of computing as a means to push forward the boundaries of brain research, cognitive neuroscience and brain-inspired ICT advances. Alongside basic research, technological advances are also lending themselves to new solutions that help patients better manage their conditions, thus leading to improvements in quality of life – wearable technology, for instance.

This is why the European Commission has been supporting brain research through successive research and innovation Framework Programmes: EUR 3.1 billion in the previous programme, FP7 (2007-2014), and another EUR 3.2 billion so far through Horizon 2020.

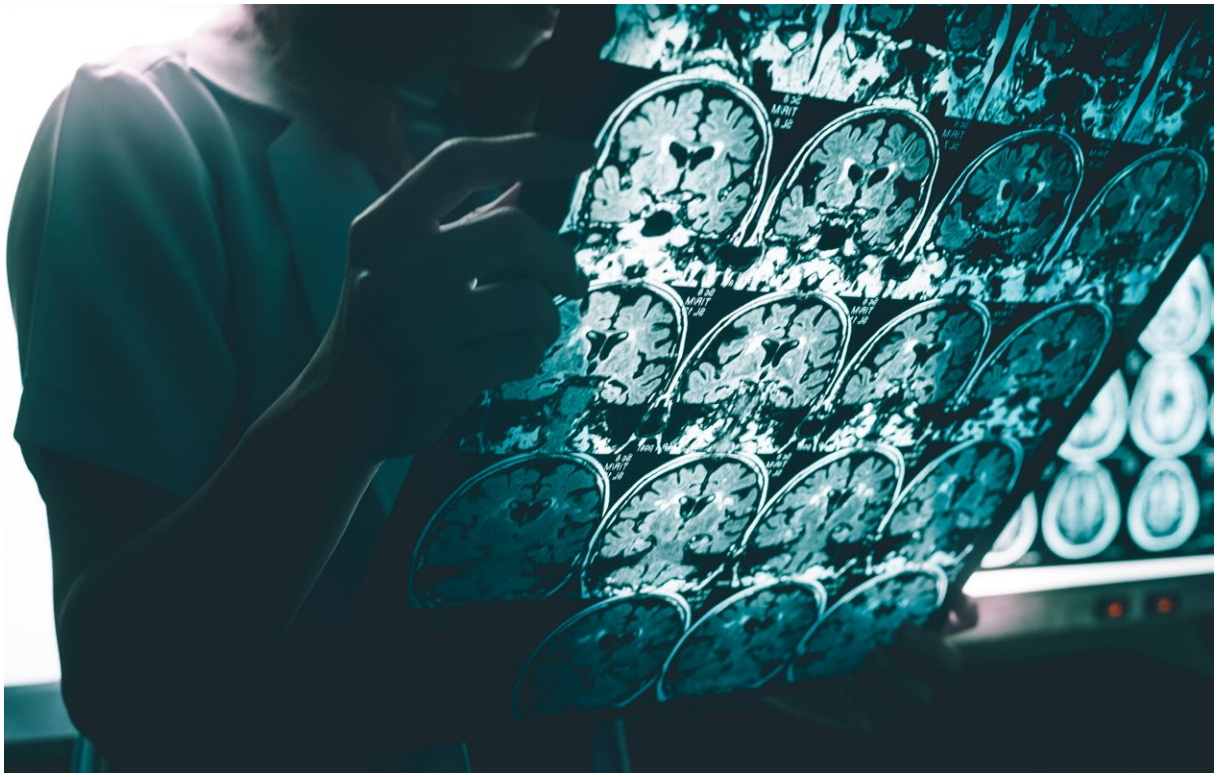
EU support for brain research spans across the various Commission funding mechanisms, from Horizon 2020's **research focus on health (indeed one of the six specific Societal Challenges addressed through Horizon 2020)** and the industry co-supported **Innovative Medicines Initiative (IMI)**, to the **European Research Council (ERC)**, the dedicated **SME Instrument** and the **Future and Emerging Technologies (FET)** programme. A selection of projects from all of these initiatives are featured together within this Results Pack.

Power to the projects

In total, this CORDIS Results Pack features 16 articles, with six dedicated to the Human Brain Project (HBP), a EUR 1 billion Flagship foreseen to be half-funded by the FET programme.

A digital disease classification system fit for the modern medical era

Classifying diseases is a practice still stuck in the past. The Innovative Medicines Initiative AETIONOMY project brings it into the 21st century.



© Atthapon Rakkthaput, Shutterstock

The classification of diseases is still largely based on patient symptoms, an approach that dates back to an era when doctors relied on spoken information and visual cues.

"You have to be aware that our current classification system for diseases has its roots in the middle of the 19th century," says Professor Dr Martin Hofmann-Apitius from the Fraunhofer Institute for Algorithms and Scientific Computing SCAI, the AETIONOMY (Organising Mechanistic Knowledge about Neurodegenerative Diseases for the Improvement of Drug Development and Therapy) project co-coordinator. "We are still following principles that go back way before we even knew what a 'gene' was."

The EU and industry-funded AETIONOMY project therefore designed a 'mechanism-based taxonomy of disease' with a particular focus on neurodegenerative diseases: namely Alzheimer's and Parkinson's. The concept was based on an intriguing idea: "If we can classify patients according to their disease mechanisms, we are in the position to predict with high accuracy whether they will benefit from a drug that targets each mechanism," says Dr Hofmann-Apitius.

A 21st century model

AETIONOMY systematically captures and represents knowledge on neurodegenerative diseases in a computable format, as a graph model that represents causes and effects and that can be analysed using algorithms. It was designed to take into account molecular biomarkers (e.g. proteins), recognising the role of personalised genomes with their individual genetic variations and including various other underlying features that have only been feasible to measure in the past few years: using neuro-imaging, for example.

Our current classification system for diseases has its roots in the middle of the 19th century.

"The real challenge, however, in this field is: nobody knows what mechanism(s) are responsible for these neurodegenerative diseases," says Dr Hofmann-Apitius. "This is why they are called 'idiopathic', to indicate that their aetiology [the cause or underlying causes of a disease or condition] is unknown."

The challenge was substantial, explains Dr Hofmann-Apitius, especially because the pharmaceutical industry partners who initiated the call wanted the new taxonomy to be validated in a clinical study, meaning demonstrating its stratifying and classification potential.

As Dr Hofmann-Apitius says, the project's goal was to explore if it was possible to identify patient-subgroups in Alzheimer's or Parkinson's disease based on disease mechanisms. "The good news is: we could demonstrate exactly that," he reveals.

A wider response

Because of the project, scientists are stepping back and starting to re-think neurodegeneration again, says Dr Hofmann-Apitius. "I am convinced: AETIONOMY has paved the way for future strategies in drug discovery and drug development in neurodegeneration research."

AETIONOMY has prepared the ground for a computational approach that drives subsequent experimental work in labs. But there is a long way to go to develop better, more efficient and cheaper drugs based on the insights and principles worked out during the project.

The project also developed the concept of 'Virtual Patient Cohorts': synthetic data sets that give a new way of sharing patient-level data without compromising the privacy of any real person on Earth. The team also gained new insights into misfolded proteins as a potential new mechanism for the 'spreading' of disease in the human brain.

The AETIONOMY concept was quite revolutionary and a bit unusual to many experimental clinical researchers and biologists, explains Dr Hofmann-Apitius, and there were several competing ideas about how a mechanism-based taxonomy could and should be constructed.

"At some point, we had to change the strategy, but finally the project – and that includes the entire consortium with all its partners – delivered on the promise," he says.

PROJECT
AETIONOMY – Organising Mechanistic Knowledge about Neurodegenerative Diseases for the Improvement of Drug Development and Therapy

COORDINATED BY
UCB Biopharma SPRL in Belgium

FUNDED UNDER
FP7-HEALTH-IMI1

CORDIS FACTSHEET
cordis.europa.eu/project/id/115568

PROJECT WEBSITE
aetionomy.eu

Neuroimaging that helps us fix our brains

In most people's minds, the purpose of medical imaging technologies is to diagnose diseases or detect them before the first symptoms occur. The BRAINTRAIN project takes another course by using functional magnetic resonance imaging (fMRI) to help patients with neurodegenerative diseases and mental illnesses in regulating their own brain.

The BRAINTRAIN (Integrative neuroscience school on brain function and disease) concept is built around that of neurofeedback training: patients can follow their brain's activity on a screen, test specific strategies to regulate it, and see the results for themselves.

Professor David Linden, project coordinator and Head of Cardiff University's neuropsychiatric imaging group, believes that this solution could help patients affected with the likes of alcohol dependency, autism, post-traumatic stress disorder or even Parkinson's disease.

What makes you think that neuroimaging can be a key weapon in the fight against mental disorders?

Neuroimaging and non-invasive neurophysiology – electroencephalography, magnetoencephalography, etc. – are presently the only techniques allowing us access to the function of the human brain *in vivo*. It is therefore a unique window into the human mind.

This window can be used to improve our understanding of the neural mechanisms behind psychiatric symptoms, for example hallucinations or drug craving, as well as to evaluate the neural effects of (psychological or pharmacological) therapies. Finally, and most importantly in the context of BRAINTRAIN, they can be used for new treatment methods, especially neurofeedback.

What would you say makes such use of neuroimaging innovative?

BRAINTRAIN brings together leading experts in real-time fMRI – a functional imaging technique that allows for tracking the activity of specific brain regions and networks at high (millimetre) spatial resolution and temporal resolution in the second range.

Prof. Nikolaus Weiskopf from the Max Planck Institute of Cognitive Neuroscience in Leipzig is an expert in ultrafast MRI, while Prof. Rainer Goebel from Braininnovation is an expert in real-time MRI data analysis. By combining these methods, we can acquire and analyse fMRI data in the sub-second range and display the signal back to the participant, which is the basis of self-regulation training. The idea is that patients can use these signals, following specific protocols, to change their brain activity, which in turn can have a positive impact on their mental health. This would be the first therapeutic application of neuroimaging.

Can you tell us more about the process involved in the treatment of a patient?

Patients are in the MRI scanner and receive feedback about their brain activity through the projection of a computer screen (it could also be auditory feedback). This computer screen could just visualise the height of activation with a thermometer or similar display, or the feedback could be provided through the change of a disease-relevant stimulus or scene, for example a food or alcohol cue as in a BRAINTRAIN study we've done on food craving.

Participants/patients are then requested to change the brain activity in a desired direction (e.g. up- or downregulate it), and they will see whether they are successful from the changes in the stimulus, which could see for instance the food picture become smaller. Learning can occur in a trial-and-error procedure, but many studies also provide some suggestions for potential strategies.

What kind of impact do you expect on patients?

A recent study from Cardiff showed substantial improvement in symptoms of depression among patients who trained in the upregulation of areas responsive to positive affective stimuli – and also in a control group training in the upregulation of a visual area.

Another study by our partners at the University of Coimbra tested the feasibility of a social attention training programme for patients with autism, using real-time processing and feedback of EEG signals to track patients' attention. This protocol trained social interaction in several contexts that are relevant to the everyday functioning of patients with autism, such as ordering a drink in a bar or talking to a teacher. Although the training programme did not produce attention improvements, it led to improvements in several clinical secondary outcome measures, especially in the domain of depression.

Can you provide other examples of disorders that could be alleviated with this method?

In addition to the examples above (depression and autism), we are looking at post-traumatic stress disorder, alcohol dependence and childhood anxiety. In other projects, we have also piloted neurofeedback for neurorehabilitation (Parkinson's disease).

How do you plan to bring this to patients?

Because of the non-invasive nature of neurofeedback, there are few obstacles to bringing this technique to patients once efficacy has been demonstrated. Of course, the availability and cost of MRI facilities constitute a constraint, but most of the protocols that we test only use a small number of sessions (1-6), which keeps costs at a reasonable level.

What has been the feedback from practitioners so far?

Practitioners were grateful for the opportunity to mention our trials to their patients. There is generally a dearth of clinical trials in psychiatry, and most patients are keen to explore new non-invasive treatment avenues, especially for disorders that are otherwise difficult to treat (e.g. alcohol dependence or autism).

Because neurofeedback involves very active collaboration of the patients who have to develop their own personalised strategies for successful self-regulation, it leads to an active learning process, and practitioners told us that they would be interested in sharing this with their patients and receiving more information about the strategies that they used. We are currently thinking about ways of capturing these strategies and incorporating them into the therapeutic process.

PROJECT
BRAINTRAIN – Taking imaging into the therapeutic domain: Self-regulation of brain systems for mental disorders

COORDINATED BY
Cardiff University in the United Kingdom

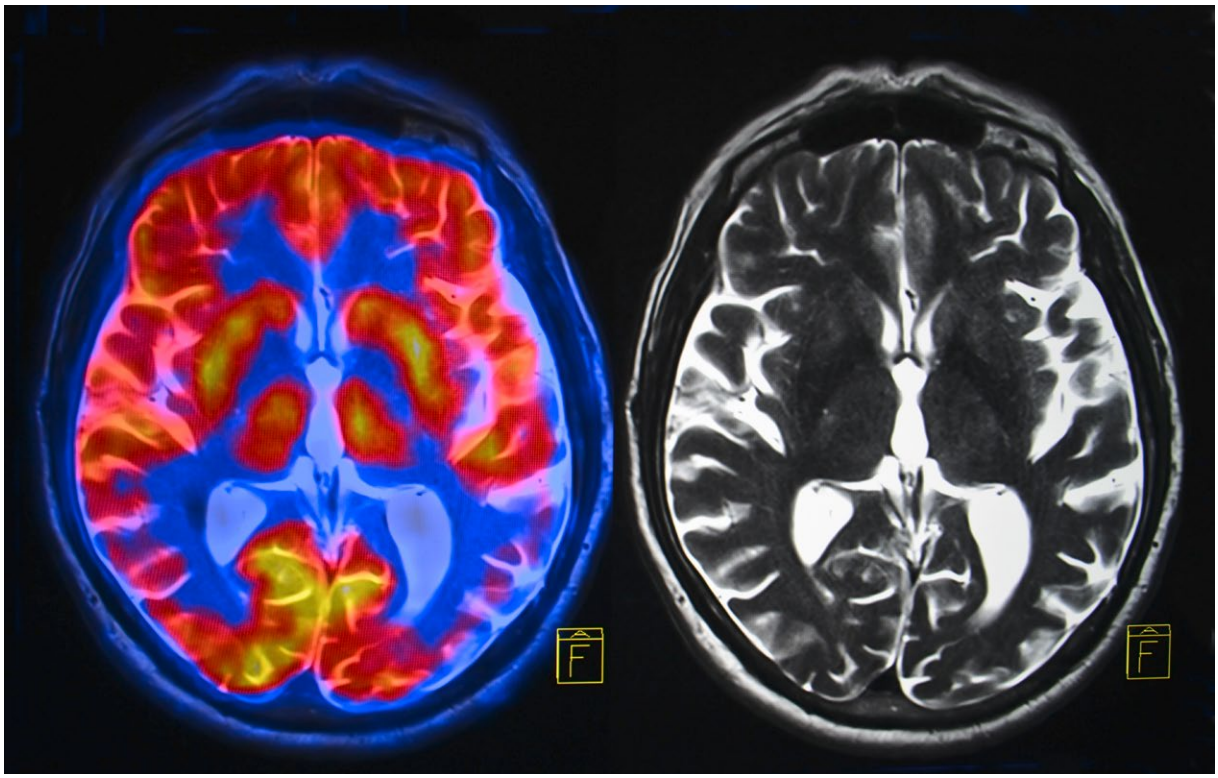
FUNDED UNDER
FP7-HEALTH

CORDIS FACTSHEET
cordis.europa.eu/project/id/602186

PROJECT WEBSITE
braintrainproject.eu

Breaking through barriers for a revolution in brain scans

Current brain scanning techniques have some critical limitations. The EU-funded BREAKBEN project broke through these barriers, promising better and more detailed brain scans.



© Semnic, Shutterstock

Brain disorders cause a great deal of suffering and a major economic burden to society. The annual cost in Europe alone has been estimated at EUR 800 billion. Now, a European team aims to put Europe at the forefront of a revolution in the scanning and measurement of the human nervous system, to improve the accuracy of current techniques that characterise electrical activity in the brain.

The BREAKBEN (Breaking the Nonuniqueness Barrier in Electromagnetic Neuroimaging) project has designed and built highly sensitive magnetometers – devices used to detect and measure extremely subtle magnetic fields. The innovative array has been designed to pick up and combine high quality signals for two principal scanning techniques for the human brain: MEG (magnetoencephalography) and ULF MRI (ultra-low-field magnetic resonance imaging).

MEG measures ultra-ultra-weak magnetic fields generated by the brain, a non-invasive method used to inform clinicians about

neuronal function. MRI maps the tissue-dependent behaviour of spinning nuclei in water molecules, giving structural images of the brain.

ULF MRI was first demonstrated in 2004 by the team of Professor John Clarke at Berkeley University, using just one sensor – known as SQUID. BREAKBEN took the idea to the next step. "We have developed the first large SQUID sensor arrays that measure both MEG and ULF MRI signals with the same sensors," explains project coordinator Professor Risto Ilmoniemi, Head of Neuroscience and Biomedical Engineering at Aalto University School of Science.

Breaking old barriers

The German physician Hermann von Helmholtz showed in the 1850s that it is impossible to uniquely determine the electric current distribution (in this case, neuronal currents) inside a conductor (in this case, the head) – even if both the electric and magnetic fields outside the conductor are perfectly known. This translated into a major future problem for scientists using MEG to measure neuronal currents in the brain, a limitation known as the non-uniqueness barrier.

"We can never be sure on the basis of MEG alone which parts of the brain are active in a subject or patient," explains Ilmoniemi. BREAKBEN's innovation is to combine these two scanning techniques to help avoid this problem, thus breaking through the barrier.

Simultaneous ULF MRI provides accurate knowledge of the location of the head and the details of the cortical shape. This allows a priori information – such as that the source current is only in the brain cortex – to be added reliably into the data analysis. This makes the scanning far more reliable.

Future applications

BREAKBEN's breakthrough opens completely different workflows for brain imaging. "We believe that we are at the edge of a qualitative technology jump with ULF MRI, its applications and combinations," says Ilmoniemi. "This will revolutionise the way we do magnetism-based measurements of the nervous system."

The technique could help with the mapping of epileptic brain activity, and ULF MRI may help perhaps even in cancer diagnostics. The MEG-MRI device will also open up brain imaging for new patient groups, such as those with metal implants. Improved workflow and more accurate diagnostics will likely shorten hospital stays and optimise treatment – thus saving on costs, too.

We believe that we are at the edge of a qualitative technology jump with ULF MRI, its applications and combinations.

The BREAKBEN team at Aalto University has received Innovation Launchpad funding from the EU to work towards commercialisation of the technique. "We are applying for further funding from Business Finland to prepare the prototype and to demonstrate its benefits in patient studies," concludes Ilmoniemi.

PROJECT
BREAKBEN – Breaking the Nonuniqueness Barrier in Electromagnetic Neuroimaging

COORDINATED BY
Aalto University in Finland

FUNDED UNDER
H2020-FET

CORDIS FACTSHEET
cordis.europa.eu/project/id/686865

PROJECT WEBSITE
aalto.fi/en

EU-AIMS: Towards personalised approaches for autistic people

The Innovative Medicines Initiative-funded EU-AIMS project has helped to signal a new era for effective therapies acknowledging the individual needs of autistic people. Its work has considerably advanced our knowledge of the variability within the biology of autistic people, identified areas for medical intervention and successfully demonstrated that compounds can modulate biological differences associated with autism.

Autistic people say that there is no one-size-fits-all approach to helping them. Some say their autism does not need treating because they value it as a key part of their identity. Others want treatment for specific aspects such as sensory difficulties or social interaction, but not at the expense of positive aspects of autism. Some prioritise treatment of conditions such as epilepsy, which they experience alongside autism.

EU-AIMS changes the playing field

The EU-AIMS (European Autism Interventions – A Multicentre Study for Developing New Medications) team has changed the playing field by showing there is no single characteristic shared by all autistic people at either the behavioural, cognitive, neurobiological or genetic levels. Instead, researchers began to identify individual neurocognitive profiles and link them to patterns of autism progression. EU-AIMS focused on developing effective treatments matched to individual needs and biological profiles and overcoming a number of research obstacles, including: Traditional approaches attempted to treat symptoms without understanding underlying causes or mechanisms; most prior studies only included 15-30 autistic people, which is insufficient to identify 'subgroups'; research into the biology of autism has lacked reliable methodologies; and clinical trials have usually included small numbers of diverse participants, limiting likelihood of success because treatments may only work effectively in some subgroups.

We started by improving knowledge of the biological diversity of autism, translated results of rodent studies to make them relevant to humans, demonstrated that certain compounds could affect the biological differences seen in autism – including in autistic adults – and searched for biomarkers that could enhance clinical trials.

The EU-AIMS project took an unprecedented multi-faceted approach. Declan Murphy, Project Lead and Professor at Kings College London (KCL) says: "We started by improving knowledge of the biological diversity of autism, translated results of rodent studies to make them relevant to humans, demonstrated that certain compounds could affect the biological differences seen in autism – including in autistic adults – and searched for biomarkers that could enhance clinical trials."

New treatment targets through genes and biomarkers

One way to identify new treatment targets is to start with genes associated with some forms of autism and ask what are their effects on the development of nerve cells and communication between them? This impacts a child's brain development and, in turn, social, cognitive and emotional development. In EU-AIMS, animal models and new non-invasive techniques, such as induced pluripotent stem cells, were used to trace causal links from genes and environmental factors to molecular changes and biological pathways. Researchers also tested whether certain compounds were effective in rodent and cellular models, thereby identifying potential new treatments based on an improved understanding of underlying biological mechanisms. A key task was then to 'translate' findings from animal models to humans by finding measures that can be safely used in humans – even babies – such as high-tech magnetic resonance spectroscopy, electroencephalogram (EEG), and respectively structural and functional MRI (sMRI/fMRI).

Another EU-AIMS focus was the identification of biomarkers. These are any objective measure, such as genes, patterns of brain activity or a test score, that predicts how a person may develop or respond to interventions. Biomarkers could be used in autism diagnosis to predict whether symptoms will change during development, and to select the best interventions, support or treatment for any given person. There were three studies with a total of over 1 200 participants, and they were assessed at a scale and in-depth level unprecedented in Europe. EU-AIMS was also the first academic/industry group to obtain 'qualification advice' from the European Medicines Agency (EMA). This crucial step improved understanding between regulatory authorities, academics and industry, and played a key role in developing new EMA guidelines on drug testing.

Next, the consortium successfully launched AIMS-2-TRIALS to continue its work, adding a programme of education and engagement, particularly for early career researchers, and a group of Autism Representatives to ensure engagement of autistic people in research.

PROJECT
EU-AIMS – European Autism Interventions – A Multicentre Study for Developing New Medications

COORDINATED BY
F. Hoffmann-La Roche AG in Switzerland

FUNDED UNDER
FP7-HEALTH-IMI1

CORDIS FACTSHEET
cordis.europa.eu/project/id/115300

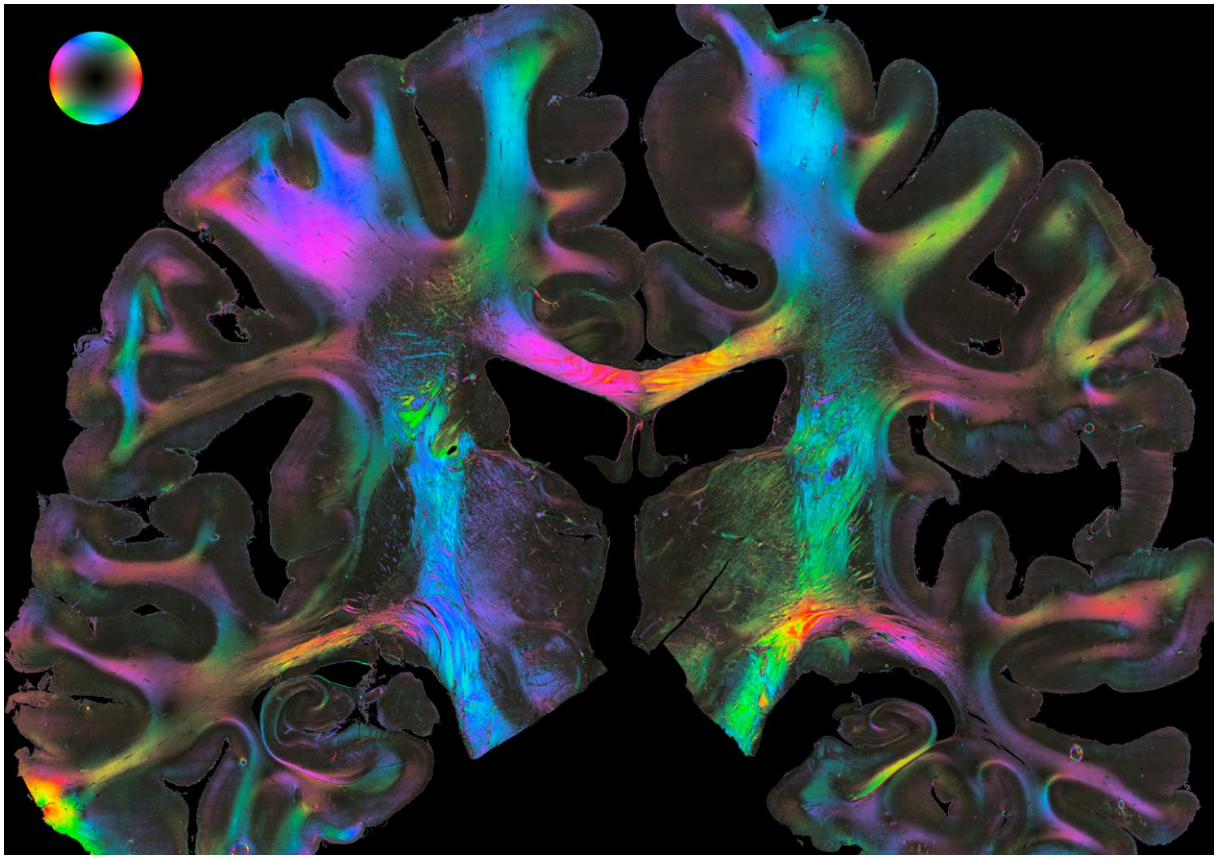
PROJECT WEBSITE
eu-aims.eu

Combining neuroscience and computing, the Human Brain Project reveals the brain's secrets

As a European Flagship Programme, the Human Brain Project (HBP) embraces ICT advances and pools distributed neuroscience and neuromedicine resources and competences. This more unified view of the brain will benefit both people and technology.

Despite many years of research, the human brain remains one of nature's greatest secrets, partly as labs have typically studied different aspects of it independent of each other.

The HBP was set up to build a unique European technology platform for neuroscience, medicine and advanced information and communication technologies (ICT). By linking research areas on an



unprecedented scale, it seeks to unlock synergies and accelerate progress.

One of the EU's most ambitious projects

The project's twofold vision is mutually reinforcing: To utilise advanced ICT in neuroscience to better understand the brain and its diseases, while drawing inspiration from biology to improve ICT.

With more than 500 scientists from 120 European partner institutions across 19 Member States, the HBP is one of the largest projects ever funded by the EU. The project has an initial run of 10 years (2013-2023) during which it will create a permanent European neuroscience research infrastructure.

"To meet emerging challenges, we've seen a shift from single specialised labs to larger interdisciplinary initiatives," says Prof. Katrin Amunts, the Scientific Research Director of the project. "This is partly due to computer-intensive simulations and the data quantities involved, terabytes to petabytes, beyond the capacity of a single research institution."

Brain complexity is breath-taking as it encompasses vastly different spatial and temporal scales, from the molecular level of synapses, cells and nerve fibres to connections between whole brain areas, and from milliseconds to whole life spans.

To enable a comprehensive understanding of brain complexity and apply it to neuromedicine, computing, robotics and AI innovations, data sharing according to FAIR principles plays a pivotal role in the HBP.

The HBP approach integrates the experimental investigation of mouse and human brain organisation, along with cognitive and theoretical neuroscience. These benefit six technology-driven platforms in the fields of: neuroinformatics, simulation, high-performance analytics and computing, neuromorphic computing, neurorobotics and medical informatics.

"Brain complexity is breath-taking as it encompasses vastly different spatial and temporal scales, from the molecular level of synapses, cells and nerve fibres to connections between whole brain areas, and from milliseconds to whole life spans," says Prof. Amunts.

As advances in neuroscience and computing can be such emotive topics, prompting philosophical questions about the 'self' and the responsible use of new technologies, the HBP adheres to Responsible Research and Innovation (RRI) principles through its ethics and society research area.

Tackling brain disorders, while developing competitive ICT

The HBP has already developed a number of new approaches for technology-driven neuromedicine.

One example is a new personalised brain avatar that has been developed to improve epilepsy surgery, soon to be tested in a 400-patient clinical trial. Another is the creation of the most comprehensive 3D human brain atlas to date.

Two of the world's leading neuromorphic (brain-inspired) computing systems, SpiNNaker and BrainScaleS, have been developed under the HBP. The project has also established the FENIX infrastructure, a Europe-wide network of supercomputing centres for the exchange of large-scale data.

"We are laying the foundations now with a broad external user community for the integrated European research infrastructure. This means building not only hardware and software, but also a culture of usage," says Prof. Amunts.

The six platforms, first made available to the public in 2016, already allow scientists access to a range of resources, including different brain models and atlases. External users can access the research infrastructure from anywhere in the world via a common web portal. For all users, a High Level Support Team is on standby. Scientists can also upload their own data with help from a curation team.

PROJECT
Human Brain Project Flagship

COORDINATED BY
EPFL in Switzerland

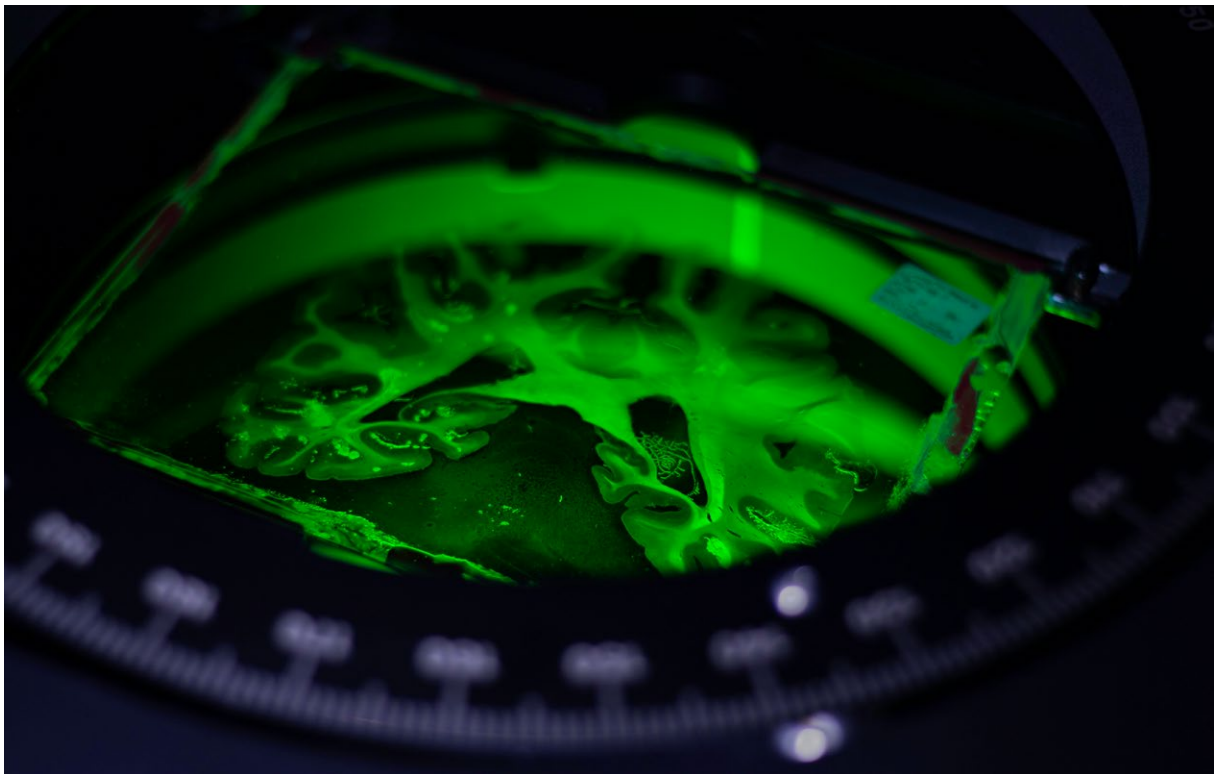
FUNDED UNDER
H2020-FET

CORDIS FACTSHEET
cordis.europa.eu/project/id/785907

PROJECT WEBSITE
humanbrainproject.eu

Collaborative data underpins advancing knowledge about the brain

The HBP's data 'ecosystem' comprises software solutions for information collection, organisation, analysis and sharing, enabling models and simulations to be built. These depend on the brain's structure and functions being mapped, from molecular to the whole brain level.



Talking of 'mapping' the human brain doesn't really do the endeavour justice. Unlike say the liver – which contains fewer cell types, organised similarly across the organ – the brain is very inhomogeneous and tremendously more complicated. This makes not only description and location vital, but also capturing interactions.

Given the scale and scope of the Human Brain Project's (HBP) ambition, a unique characteristic is the broad range of expertise available. This is critical, since outputs rely on productive interactions among these very different communities of researchers and developers, impossible to achieve working in isolation.

"These interactions do present challenges on a scale possibly not seen by any other European project," says Prof. Jan Bjaalie. "There are barriers created by different practices, with everyone bringing traditions from their own fields, and there are terminology barriers. These barriers actually explain the rationale for the HBP, while highlighting the importance of getting the data infrastructure right."

Developing a generic data system

Neuroscience has typically not managed and shared data at the large scale of the HBP, partly as the focus has previously been on the publication of papers which interpret collected data. For the HBP to capitalise on research synergies across all areas of neuroscience, the project's data has to be collaborative.

Infrastructure developments go hand in hand with the science, enabling researchers to find and access relevant data, use it in clearly defined conditions, share the results, and cite the work of the original data providers.

The data is stored alongside metadata tags and is searchable through a web browser. Specific features within particular groups of data can be extracted for incorporation into computational models and these can be used to perform simulations, with the results compared to data from real brain experiments.

"Infrastructure developments go hand in hand with the science, enabling researchers to find and access relevant data, use it in clearly defined conditions, share the results, and cite the work of the original data providers," says Prof. Bjaalie.

Given the quantities of data involved, these efforts are only possible thanks to the use of high performance computing.

New technologies and clinical applications

The three primary goals of the HBP are: to better understand how the different elements of the human brain's organisation fit and work together (basic science), to translate this to better diagnoses and treatments of brain disease (applied science for health), and also to use this understanding to develop new brain-inspired technologies (technology).

Within these broad goals researchers are guided by some overarching research targets. Dementia, in particular Alzheimer's disease, has been chosen as an area to demonstrate the Medical Informatics Platform's functionality, installed at hospitals across Europe. Combining this anonymised clinical data facilitates more efficient analysis.

Another example is the use of personalised brain models and atlases, navigable in 3D, for different applications like better planning for epilepsy surgery or deep brain stimulation in Parkinson's. Identification and resection of a small portion of the brain where epileptic seizures originate requires a deep understanding of the seizure's organisation. To improve these procedures, the HBP combines a new multi-scale modelling and simulation environment with the project's brain atlases and other data analysis tools.

Critical to achieving the goals of the HBP is that it makes its systems openly available to the wider research community. Forthcoming this year will be a new online portal providing access to a series of user-centric services. "While some of the information is already available it is not so visible or easy to navigate. The new portal will make it easy for the outside community to find and use the tools and services delivered by the HBP," says Prof. Bjaalie.

PROJECT
Human Brain Project Flagship

COORDINATED BY
EPFL in Switzerland

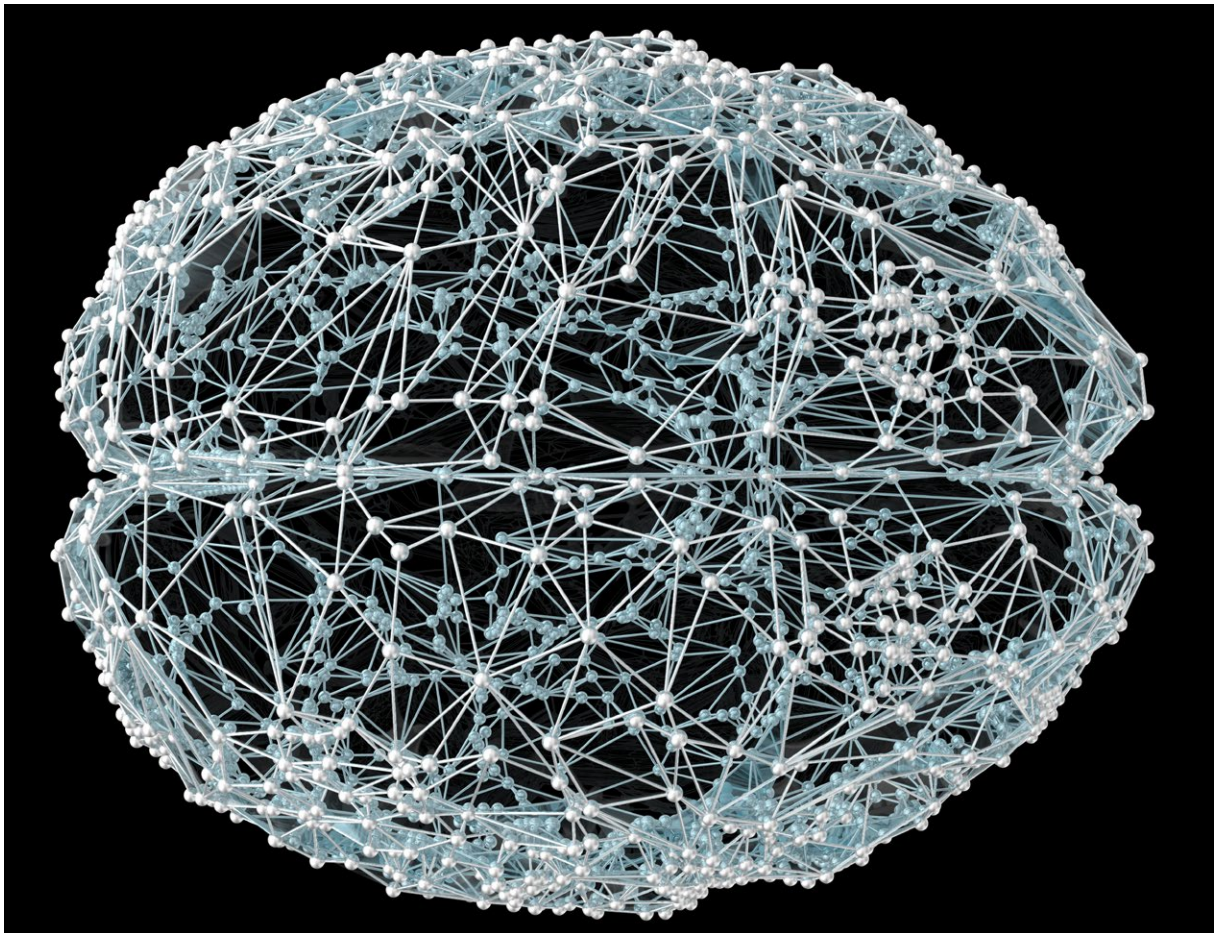
FUNDED UNDER
H2020-FET

CORDIS FACTSHEET
cordis.europa.eu/project/id/785907

PROJECT WEBSITE
humanbrainproject.eu

Understanding how the brain's structure and functions generate consciousness

Definitions and understandings of consciousness have been hotly contested down the centuries, engaging philosophers and more recently neuroscientists. To make further sense of it all, the HBP models both the neurological 'wood and the trees' simultaneously.



How is it that the same anatomical structure, our brain's intricate network called the 'connectome', can at times host the complexity of consciousness and at other times exist seemingly as dull matter? This is one of the greatest mysteries of biology, or even physics.

If we take a broad definition of consciousness as experience of ourselves and the outside world, it can be said to come and go. During dreamless sleep it seems absent, seemingly reappears during vivid dreaming, before more definitively reappearing on awakening. But how the brain transitions between these states is poorly understood.

Acknowledging that answers may lie within neuroscience, one of the objectives of the Human Brain Project (HBP) is to develop a complex model characterised by realistic connectivity, detailed neural dynamics and learning rules; one undertakes multiple cognitive tasks by integrating different cortical areas.

Replicating basic activity and cognitive tasks

The 'Network models for consciousness' programme within the HBP set out to better understand the relationship between structure and function in the brain, to explain the emergence of the complex network dynamics which enable perception, prediction, goal directed behaviour and other higher-end cognitive functions.

"How is it that the same anatomical structure, our brain's intricate network called the 'connectome', can at times host the complexity of consciousness and at other times exist seemingly as dull matter? This is one of the greatest mysteries of biology, or even physics," project researcher, Prof. Marcello Massimini, says.

One of the challenges of building a realistic, data-driven, multitasking consciousness model is that of getting the right structural and functional modelling parameters to replicate the emergence of balanced, complex patterns of activity. "Existing models replicate either specific cognitive functions or global brain states, but can't cope with both. This balance between differentiation and unity is what makes the brain special with respect to consciousness," says Prof. Massimini.

The programme benefits from the unique range of HBP expertise to build a model using a common infrastructure assembled from several assets including: atlases, neuroinformatics, brain simulation, high-performance analytics and computing, medical informatics and neuromorphic computing.

This 'backbone' collects, curates and integrates structural and functional data on a scale ranging from single neurons to the whole brain. Incorporating both high-level, large-scale models that replicate global brain dynamics (top-down) and detailed, biophysical models of realistic neuronal functioning (bottom-up) will be a key step.

Medical implications and beyond

The project's results, combined with others from the HBP, are forming a more coherent picture. For example, empirical research with rodents has identified a key neuronal mechanism for the conscious perception of sensory stimuli. This process, known as 'apical dendritic amplification', was also detected in the visual system of humans and can be replicated in computer simulations as well as in neuromorphic chips to improve image recognition.

In parallel, these activities have elucidated the mechanisms by which recurrent, complex cortical interactions are disrupted upon falling asleep, whereby neurons cannot keep track of the inputs they receive.

"Thanks to our common infrastructure, two lines of research may soon incorporate a unifying mechanism, accounting for both sensory perception of specific content and global brain state transitions," says Prof. Massimini.

This work has significant medical implications for assessing patient consciousness and treating disorders, contributing to bedside observation during loss and recovery of consciousness in sleep, anaesthesia, coma and related states. Currently, there is a lack of clear brain-based behavioural guidelines; crucial in intensive care medicine.

The results are also of relevance for brain-machine interfaces such as those for sensory function restoration, as well as for future AI architectures.

PROJECT
Human Brain Project Flagship

COORDINATED BY
EPFL in Switzerland

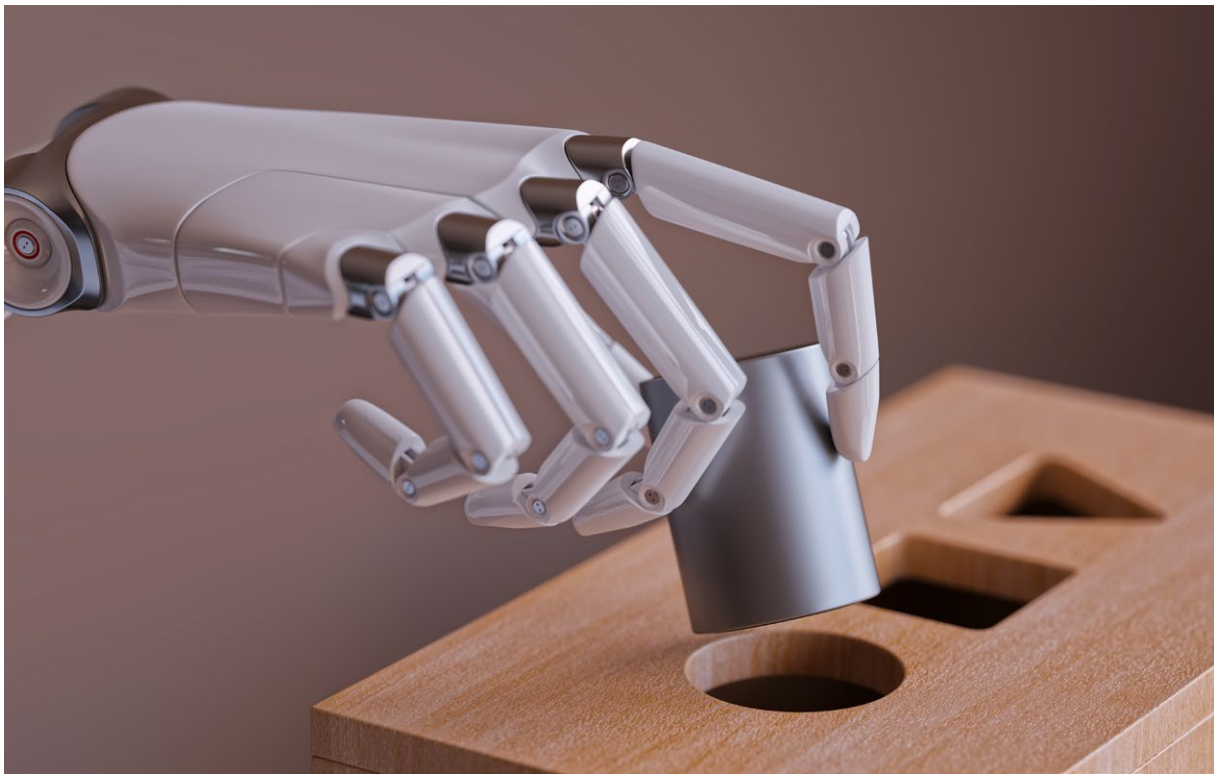
FUNDED UNDER
H2020-FET

CORDIS FACTSHEET
cordis.europa.eu/project/id/785907

PROJECT WEBSITE
humanbrainproject.eu

When virtual brain models meet real and simulated robot bodies

A crucial part of what gives the brain its power is its ability to learn from the interactions of the body under its control with the world. Neurorobotics research offers a unique opportunity to understand how this action-perception loop works, and to use this knowledge to build the next generation of robotic systems.



The Human Brain Project's (HBP) Neurorobotics Platform (NRP), is a set of tools to connect and simulate brain and body together ('embodiment'). It supports virtual experiments in physically realistic simulated environments through which neuroscientists can evaluate functional performance of brain models in the context of behavioural tasks, and so compare or refine them iteratively. This provides researchers with new tools to study topics such as neural control of movement or learning mechanisms in the context of interactions with the environment. Eventually, the knowledge derived from these studies will fundamentally change the way robots are designed.

Better understanding brain structure, function and dynamics

The first step for embodied simulation is to define a task to be performed and establish the relevant virtual and robotic setup. Next, a control architecture (brain) for the simulation is selected, alongside the relevant learning paradigms and experimental scenarios. The NRP supports users at every step of this process.

Virtualisation of neuroscience is the natural next step, where the limits are those imposed by computation power. In other words: the sky is the limit!

The closed-loop experiments then afford neuroscientists a unique opportunity to explore the relationship between brain structure, function and neural dynamics in specific behavioural contexts. For example, several HBP partners are jointly investigating how oculomotor activity, visual processing and dexterous motor control work together in tasks that involve grasping moving objects. Others are creating a virtual mouse for the NRP, complete with a highly-detailed musculoskeletal system; the objective is to create a virtual model that is as close as possible to its biological counterpart, so that some animal experiments can be reproduced and carried out virtually.

These advances may eventually provide significant benefits for medical science. For example, members of the HBP team are modelling the neural circuitry of the spinal cord and simulating it in order to understand how spinal stimulation can be optimised and/or personalised. One of the principal aims is to assist patients with spinal cord injuries in recovering some capacity for locomotion, and neurorobotic developments could prove invaluable here.

Building better robots

Other experiments aim to unlock the secret of the biological processes that enable the brain to adapt behaviour to changing environmental conditions. This would provide researchers with the means to build better robots, increasing their effectiveness in areas where the current state-of-the-art is found lacking, such as with situational awareness.

Additionally, the NRP provides all the simulation tools required to train robotic systems in simulation: not only does this minimise the risk of damage to expensive hardware, it also opens up the possibility of using massively parallel training algorithms.

"Using High Performance Computing will greatly reduce the time needed to train robotic systems. Additionally, virtual prototyping of robotic platforms should reduce development costs and deliver better designed, more robust products," says Prof. Dr. Alois Knoll, project leader for the NRP.

Some HBP partners are now investigating whether brain-inspired cognitive architectures may be useful as control systems for industrial robotic arms operating in collaboration scenarios (cobots). They also extend these research efforts to mechanically-compliant robots, which could provide 'safety by design' where robots must operate around humans – in factories for example.

The NRP is public, online and available for researchers who want to test their brain models or to build the brain-inspired robots of the future. "Virtualisation of neuroscience is the natural next step, where the limits are those imposed by computation power. In other words: the sky is the limit!" concludes Prof. Dr. Knoll.

PROJECT
Human Brain Project Flagship

COORDINATED BY
EPFL in Switzerland

FUNDED UNDER
H2020-FET

CORDIS FACTSHEET
cordis.europa.eu/project/id/785907

PROJECT WEBSITE
humanbrainproject.eu

Shaping the ethical direction of the HBP for the public interest

Better understanding the human brain offers insights into what it means to be human, the causes of brain-related diseases – alongside improved diagnosis and treatment – while holding out the prospect of advances in artificial intelligence technologies. But at what ethical cost?

Sensitive to the ethical questions emanating from the research methodologies, results and potential applications at the interface of neuroscience and technology, the Human Brain Project (HBP) incorporated a programme of Responsible Research and Innovation (RRI).

By engaging with external stakeholders, including citizens, the RRI programme studies specific research consequences, while continuing to address traditional ethical concerns surrounding issues such as animal or human experimentation. The work contributes to the governance of the HBP as a whole, for example by developing standard operating procedures. It also ensures ethical issues can

be identified, raised and responded to, through formal and informal channels, including an independent Ethics Advisory Board (EAB).

Ethics without borders

Ethics touch almost all aspects of most research projects, but the scale and ambition of the HBP make ethical implications more pronounced. Taking data governance, and questions about which data can be used for what purpose and by whom, generates a range of legal as well as ethical concerns. With the HBP, exchanging data across national borders adds a further layer of complexity.

In response, the HBP Ethics and Society research programme led by Prof. Kathinka Evers has established a working group which collates all data-related policies and regulations. "This is a large and multi-faceted problem that all large data-intensive projects share. Our work in this field is seminal, with potential to shape how future international collaborations work," says HBP's Ethics Director Prof. Bernd Stahl.

Another crucial area of work relates to policy and regulatory compliance. In some cases, pre-existing EU regulations make the rules clear. "With biomedical research for example, EU rules about animal protection, along with means of enforcement, are well established," says Prof. Stahl. "In other less defined areas of research, the EU has a clear role to lead a broader social debate."

In most cases there is not one single, simple answer to ethical questions and there is no final ethical arbiter. We encourage open, inclusive and transparent communication to reach consensus about how to best move forward.

One such area is that of artificial intelligence (AI). While the HBP's neuromorphic research may hold the key to developing stronger AI, the roll out of ever-increasing AI capabilities could prove socially problematic. Within the field of employment alone it has the potential to create unemployment in some sectors, while also increasing workplace discrimination and bias.

The ethics and society programme contributes to these social debates with its own public engagement activities, led by The Danish Board of Technology. The programme also conducts empirical investigations through interviews, surveys and public engagement exercises.

The practical and the profound

The HBP research will benefit science, ICT and medicine in innumerable ways, with important implications for citizens. Novel neuroscience-inspired technologies, such as neuromorphic computing and neurorobotics could fundamentally alter the physical and cognitive capabilities of humans.

Perhaps the biggest, but most challenging, impact will come with the development of better ways of understanding, diagnosing and treating brain-related diseases. On a more philosophical level, better brain understanding may affect the way we think about ourselves, exerting a profound influence on social structures and relations.

Forewarning that those implications are likely to be both negative and positive, means that the right questions can be asked, in time, by the right people.

However, as Prof. Stahl says, "in most cases there is not one single, simple answer to ethical questions and there is no final ethical arbiter. We encourage open, inclusive and transparent communication to reach consensus about how to best move forward."

PROJECT
Human Brain Project Flagship

COORDINATED BY
EPFL in Switzerland

FUNDED UNDER
H2020-FET

CORDIS FACTSHEET
cordis.europa.eu/project/id/785907

PROJECT WEBSITE
humanbrainproject.eu

The Virtual Brain simulates the brain to reveal the origins of disorders

The human ability to use a 'tool' (our brain), to build another tool to explain the workings of the first tool, is an evolutionary gift that distinguishes us from other animals. Powerful simulation engines like 'The Virtual Brain' exemplify both this gift, as well as its unwrapping.

A cognitive irony is that the human brain's very complexity makes it difficult to theorise about its workings, using thought alone. However, computer models can simulate the consequences of theories, identifying problems and formulating new theories for neuroscience testing.

Within the Human Brain Project (HBP), large-scale brain simulation, and specifically the included Virtual Brain, affords a better understanding of the emergence of so-called resting-state networks. Electroencephalography (EEG) and magnetic resonance imaging (MRI) show that brains are active even when not engaged in specific activities. Brain simulations explain these rhythmic networks as spontaneously emerging from the interaction of large groups of nerve cells via the brain's white matter.

Looking for emergent patterns

The brain is on average made up of approximately 86 billion nerve cells and 1 quadrillion connections between them. Nerve cells and connections are in turn made up of even smaller elements, such as ion channels and spines, with a range of functional properties. Simulating the brain down to this level would require the measurement of all the subtle properties of these components.

But computer processing power is still too limited to perform these calculations in a practical amount of time. On HBP's Brain Simulation Platform (BSP), teams work with simulation engines on different levels of abstraction – from modelling smaller volumes to a high level of detail to more coarse-grained, but still full-brain simulations of brain dynamics. One of the latter is The Virtual Brain, "So, we are not trying to accurately simulate the brain, but rather reveal the large-scale patterns that emerge from the interaction of these elements, like those that emerge in a flock of birds," says Prof. Petra Ritter, leading the work on the Virtual Brain Project and connecting it to more detailed simulators on the BSP.

Dividing the entire brain into areas, the researchers formulate theories testable by computer modelling. As many details are little understood or only vaguely specified, they use EEG and fMRI brain imaging to constrain the models. These simulations enable the team to estimate the connectivity between brain areas yielding so-called connectomes (strengths of interaction between different brain areas) and so accurately predict brain activity.

"We are interested in high-level cognitive functions like intelligence, decision-making, memory and learning, to work out the cause of impairments and to map out improvement strategies," says Prof. Ritter.

So far, amongst other findings, the project has increased understanding about: recovery after stroke, the prediction and characterisation of epileptic seizures, the progress of Alzheimer's and the functional implications of brain tumours.

The open source Virtual Brain is freely available for download and even modification.

The hope of the 'virtual human'

Neurodegenerative disorders are one of the most pressing problems facing modern societies. In addition to the individual burden, with 14 million people across Europe predicted to have dementia in 2030 alone, the cost is predicted to surpass EUR 250 billion by that year.

Additionally, mental health conditions such as bipolar disorder, schizophrenia, depression, anxiety, PTSD, ADHD, alcohol and drug use disorders currently affect one in six people across the EU, and this percentage is rising. The cost of healthcare, social security and decreased employment/productivity is EUR 620 billion annually. Existing treatments for these conditions usually rely on medication, which suppresses symptoms rather than cures illness.

We are interested in high-level cognitive functions like intelligence, decision-making, memory and learning, to work out the cause of impairments and to map out improvement strategies.

While the underlying mechanisms of these disorders remain unclear, evidence increasingly points to complex systematic physiological connections, which are hard to study with experimental methods alone. "With full-brain simulation, and in the future full-body simulation, we will better understand the whole human system. 'Virtual humans' would allow us to develop customised interventions targeting the combination of genetic, metabolic and neuronal factors responsible for brain disorders," concludes Prof. Ritter.

PROJECT
Human Brain Project Flagship

COORDINATED BY
EPFL in Switzerland

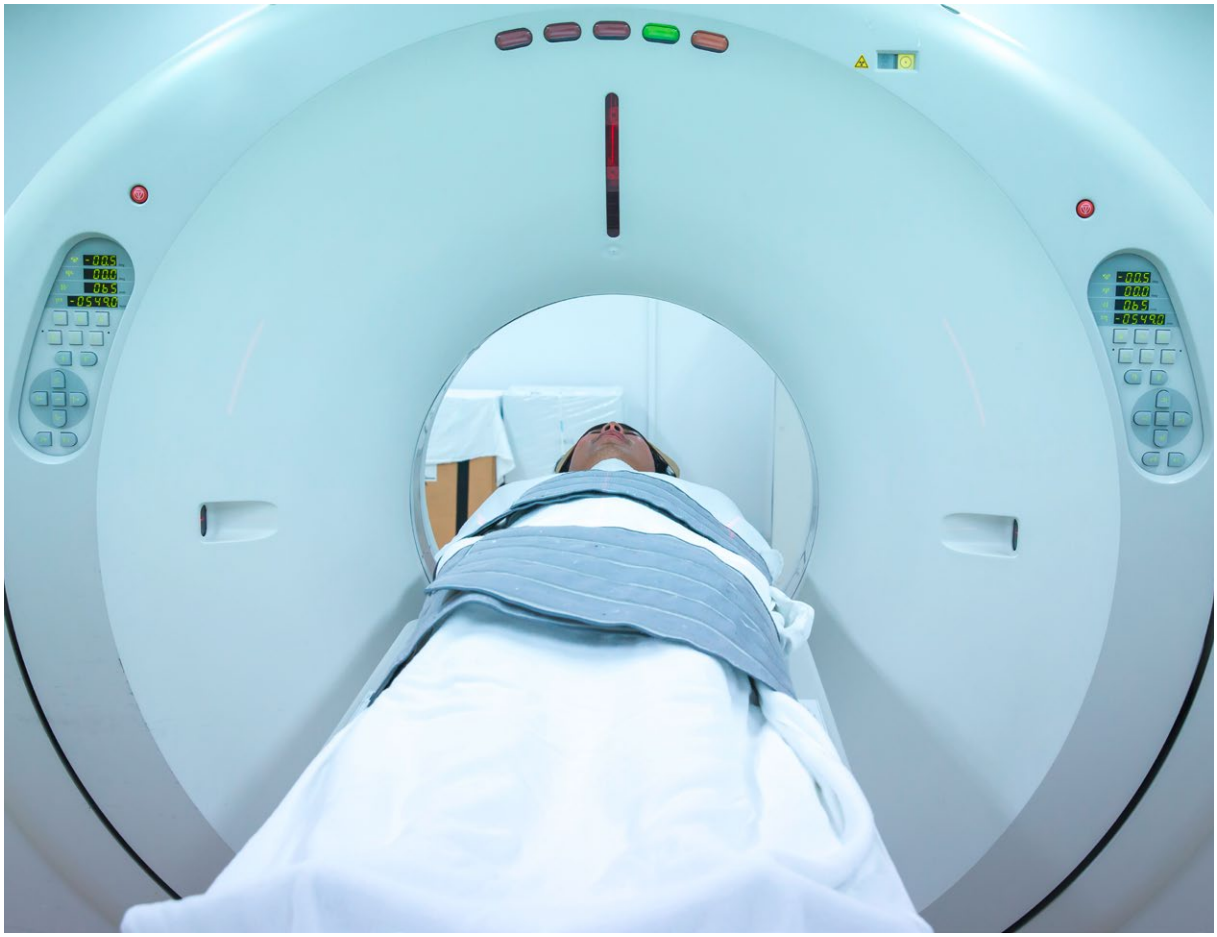
FUNDED UNDER
H2020-FET

CORDIS FACTSHEET
cordis.europa.eu/project/id/785907

PROJECT WEBSITE
humanbrainproject.eu

A high-performance PET scanner for integration into current MRI systems

Although it's mostly known for its key role in detecting cancer and monitoring its evolution during treatment, PET imaging actually has a multitude of other clinical applications. Neurology is one of these. The MINDView project recently tapped into its potential by developing a compact brain PET imager that can be combined with existing MRI systems to better diagnose schizophrenia.



Besides its high resolution and efficiency, the main advantages of MINDView's (Multimodal Imaging of Neurological Disorders) new PET imager are its significantly reduced cost, its size and the fact that it allows for conducting both Positron Emission Tomography (PET) and Magnetic Resonance Imager Radio Frequency (MRI RF) imaging at the same time.

"MRI and PET provide complementary information," explains Prof. Jose Maria Benlloch Baviera, coordinator of the project and Director of the CSIC's Institute for Instrumentation in Molecular Imaging (I3M). "MRI provides high quality and resolution images on the morphology of the soft tissue, which is very useful in localising lesions in the body. On the other hand, PET images provide information on the physiologic processes occurring in different organs and substructures. The two technologies potentiate each other: For instance, MRI information can be used to better position physiologic information from PET within the brain."

Smaller clinics that cannot afford a new whole-body PET/MRI system might even be able to finally acquire this powerful technology.

The potential for the precise and early diagnosis of mental disorders such as schizophrenia and severe depression is tremendous. Neurotransmitter pathways-specific PET radiopharmaceuticals – such as glutamatergic, serotonergic or dopaminergic – can be imaged, while areas of the brain activated by performing a task are tracked with functional MRI. According to Prof. Benlloch Baviera, this might eventually lead to precise and quantitative diagnosis of mental disorders that would be impossible to obtain with currently available techniques.

MINDView's PET system also stands out through its design. Compared to current devices made of thousands of small crystal pixels coupled to an array of photo-sensors, this one includes only 60 large monolithic crystal blocks coupled in one side to a matrix plane of silicon photo-sensors. "This design has several performance advantages. Since the same amount of light is emitted in all directions, we can determine the depth of gamma ray interactions by measuring the width of the light distribution. In other words, we can find the 3D position of the gamma ray impact. This is a critical feature to avoid image blurring when using scanners that are close to the organ. Besides, light is directly detected by the sensors instead of bouncing back and forth in the pixel. This allows in principle for better energy and timing resolution, which in turn reduces signal noise at the image," Prof. Benlloch Baviera explains.

Such design also brings cost down considerably, as tasks such as cutting, polishing, painting and gluing thousands of pixels back into a single block are avoided. This is a major incentive for hospitals which generally must pay between EUR 4 and 7 million for commercial PET/MRI systems. Smaller clinics that cannot afford a new whole-body PET/MRI system might even be able to finally acquire this powerful technology.

Last but not least, the new design allows for a portable system that can easily be removed when it's not needed for a particular MRI examination. As Prof. Benlloch Baviera points out, this represents a major technical breakthrough since the mutual interference of MRI and PET imaging modalities, in particular when being physically so close to each other, would normally be substantial.

"For instance, the high field (3 Tesla) produced by the main magnet of the MRI may completely degrade the performance of the photo-sensors and electronics of the PET scanner. Special photo-sensors based on silicon technology have been developed and non-paramagnetic electronics and connections have been used in order to avoid that effect," he explains. "Furthermore, innovative shielding of the PET modules and the RF coil have been designed to avoid eddy currents that will distort the high homogeneity of the magnetic field required for a top-quality MRI image."

The device is currently being tested on patients with Alzheimer's disease (AD).

PROJECT
MINDVIEW – Multimodal Imaging of Neurological Disorders

COORDINATED BY
Spanish National Research Council in Spain

FUNDED UNDER
FP7-HEALTH

CORDIS FACTSHEET
cordis.europa.eu/project/id/603002

PROJECT WEBSITE
mindview.i3m.upv.es

Wearable devices to help prevent sudden unexpected death through epilepsy

To this day, little is known about sudden unexpected death in epilepsy. Only very few cases have actually been witnessed or monitored. But that might be about to change. Wearable electronics could provide just the solution researchers have been looking for.

According to the WHO, 300 000 new cases of epilepsy are diagnosed each year in Europe. And while several treatments do exist, the risk of sudden unexpected death (SUDEP) is still very high, with a UK government report showing that SUDEP is responsible for 33 000 deaths in Europe each year, of which 40 % are preventable. To prevent it, researchers first need constant physiological monitoring of patients on which to base their investigations. This requires a non-invasive system that patients could realistically carry with them at all times, without compromising on the device's performance.

"A 'truly wearable' solution – that is, non-invasive, easy to use, comfortable, small, requiring low maintenance and durable – is needed. And if such a device could provide reliable signals, accurate biomarkers and even accurate identification of potentially dangerous situations, then it would be a game changer," says Esther Rodriguez-Villegas, Professor in Low Power Electronics at Imperial College London.

The purpose of the European Research Council's (ERC) NOSUDEP (A Wearable Electronics Approach To Reduce Mortality in Epilepsy) project, which is led by Prof. Rodriguez, is to adapt devices developed under the previous ERC WEEG and One-EG projects (respectively for electroencephalography and sleep disorder monitoring purposes) to these requirements.

A number of trade-offs

NOSUDEP's success will be a matter of trade-offs: devising a handy solution, while at the same time ensuring optimal data rate transmission and high accuracy. And as the stakes are much higher than with commercial applications, there is also little margin of error. As Prof. Rodriguez explains: "If any of the algorithms end up leading to false warnings to the patient, it is just not good enough for the detection of potentially dangerous situations. We are talking about devices that patients will need to wear for extended periods of time. False alarms would quickly result in patients' non-compliance. Our research focuses on algorithms that keep these constraints in mind."

False alarms would quickly result in patients' non-compliance. Our research focuses on algorithms that keep these constraints in mind.

Another major challenge lies in how the project aims to sense as many physiological parameters as possible from just one location in the body. Likewise, a small device implies very low power consumption, which in turn limits the possibilities of optimising the sensing process.

Building on previous projects

Although the project is still in its early stages, it can build upon previous successes of Dr Rodriguez and her team. Research under the One-EG project had already enabled them to create a sleep monitoring device 20 times lighter and 50 times smaller than alternatives, with an accuracy similar to non-wearable systems.

The WEEG project, on the other hand, had already tackled the most important technological challenges related to power consumption. Its new generation of algorithms is embedded in novel integrated circuits that can be incorporated in electrodes and consume extremely low levels of power. This system also decreases the amount of data provided to the doctor for diagnosis, which has the additional advantage of reducing unnecessary burden.

Before NOSUDEP, the successful work of Prof. Rodriguez had already led to the creation of a start-up company. The latter is now in the last steps of the regulatory process to commercialise the first wearable medical device for automatic diagnosis of sleep apnoea. If NOSUDEP succeeds in its mission, Dr Rodriguez hopes that they will be able to do the same for epilepsy patients. "I also hope that this project will manage to shed more light on the mechanisms of SUDEP, and further down the line even help prevent it," she concludes.

PROJECT

NOSUDEP – A Wearable Electronics Approach To Reduce Mortality in Epilepsy
ONE-EG – Wearable Brain Monitoring Technology for Quick Diagnosis of Sleep Disorders
WEEG – 'Chips on the go': towards truly wearable EEG systems

HOSTED BY

Imperial College of Science, Technology and Medicine in the United Kingdom

FUNDED UNDER

H2020-ERC
FP7-IDEAS-ERC

CORDIS FACTSHEET

cordis.europa.eu/project/id/724334
cordis.europa.eu/project/id/679417
cordis.europa.eu/project/id/239749

ERC research lends an ear to the voices heard by schizophrenia patients

The ERC-funded ONOFF project is building upon previous efforts to better understand auditory hallucinations (AH) in patients with schizophrenia. Its results could lead to new cognitive and pharmacological treatments.

In 70 % of cases, schizophrenia appears alongside AH. Patients start hearing one or more voices inside their head, and they would often describe how these voices keep arguing with them or telling them what to do.

From VOICE to ONOFF

Prof. Kenneth Hugdahl's research taught us that the perception of these voices found a neuronal origin in the temporal lobe on the left side of the brain. And he has kept advancing the scientific understanding of this symptom ever since. Under the VOICE project – completed in 2015 – Prof. Hugdahl notably obtained a first glimpse at the neurochemistry of AH. He uncovered how its onset was accompanied by hyper-excitation in voice areas and hypo-activation in the inhibition areas of the brain. Now, with its second ERC Advanced grant for ONOFF (Perception of voices that do not exist: Tracking the temporal signatures of auditory hallucinations), the Founder of Bergen fMRI Group is trying to explain one of the most intriguing characteristics of AH, its fluctuation over time.

"Following the findings of the VOICE project, it struck me that most, if not all research efforts have so far focused on explaining what caused the onset of a hallucinatory episode," Prof. Hugdahl explains. "What I observed, however, was that hallucinatory episodes seem to fluctuate over time. For me, it was clear that if the onset of an episode had neurobiological markers, it was also possible that the offset of an episode could have corresponding markers, although for some reason the process was reversed."

Since schizophrenia is a heterogeneous disorder with clinical, cognitive and brain symptoms, it is important to aim at developing new treatments at different levels of explanation, and I believe that a combination of cognitive and pharmacological treatments will have the best effects.

It didn't take much more for Prof. Hugdahl to kick-start the ONOFF in 2016. Since then, the project has seen the launch of a brief questionnaire to get information on AH fluctuations over time and a phone app asking questions related to the key dimensions of AH. It carried out the following: used a Norwegian population study on the incidence of AHs in the general population to find out about potential environmental triggers; devised a method to see if changes in brain activation (measured with fMRI) had corresponding changes in neurotransmitter levels (measured with MRS); tried out a training app for patients to increase their cognitive control over the 'voices'; and observed on and off AH fluctuations in patients within an MR scanner.

Tangible findings already

Although the project is only set for completion in 2021, it has already led to interesting results. The positive correlation between glutamate/glutamin levels in the voice areas in the brain and severity of AHs found in the VOICE project was verified. The team found a negative correlation between glutamate/glutamin levels and severity of AHs in an area of the brain's frontal lobe related to top-down cognition and inhibitory control. Thanks to the smartphone app, Prof. Hugdahl could also observe that as patients indicate that the level of distress is increasing, the feeling of cognitive control of the 'voice' is going down, and vice versa. This indicates that the use of app technology can help obtain more detailed data on the relationship between stress and control.

Eventually, ONOFF research could inspire treatment approaches to pharmacologically prolong OFF-periods by blocking hyper-excitation and/or boost hypo-excitation. Besides, the use of the dichotic listening training app could help improve cognitive control. "Since schizophrenia is a heterogeneous disorder with clinical, cognitive and brain symptoms, it is important to aim at developing new treatments at different levels of explanation, and I believe that a combination of cognitive and pharmacological treatments will have the best effects," Prof. Hugdahl concludes.

PROJECT

ONOFF – Perception of voices that do not exist: Tracking the temporal signatures of auditory hallucinations
VOICE – 'Hearing voices': From cognition to brain systems

HOSTED BY

University of Bergen in Norway

FUNDED UNDER

H2020-ERC
FP7-IDEAS-ERC

CORDIS FACTSHEET

cordis.europa.eu/project/id/693124
cordis.europa.eu/project/id/249516

New research highlights biological similarities between psychiatric and neurodegenerative disorders

The Innovative Medicines Initiative (IMI) PRISM project is proposing a paradigm shift to develop more adequate and effective treatments for neuropsychiatric disorders. The project moves away from current classification methods to focus on the patients' underlying neurobiology.

Patients suffering from schizophrenia, major depression or Alzheimer's disease share more in common than the neuropsychiatric nature of their condition. First, despite 50 years of drug research and discovery, treatment for each of these three disorders still involves the use of over 100 compounds in empirically chosen concentrations. In most cases, this results in poor efficacy and causes tolerability issues.

The second point of convergence is, unlike the former, a source of hope. It is the recent understanding from the field of aetiological research that there is more of an overlap between psychiatric and neurodegenerative disorders than previously thought. This – along with the deceleration of treatment innovation over the past decades – calls for a paradigm shift in the drug discovery process. One that would move away from a classification of disorders that largely disregards the underlying neurobiology giving rise to symptoms.

Quantifying neuropsychiatric diseases

PRISM (Psychiatric Ratings using Intermediate Stratified Markers) is pioneering in this regard. By developing a quantitative biological approach to the understanding and classification of neuropsychiatric diseases, the project aims to develop a new framework that would help physicians better inform their patients of the complexity and the optimal management of their illness. But most importantly, it has the potential to accelerate the discovery and development of better treatments.

"The main difficulty in the construction of such biologically-valid diagnoses is the lack of objective biomarkers," says Dr Martien Kas, Professor of Behavioural Neuroscience at the University of Groningen and PRISM co-project coordinator. "Moreover, the disconnect between diagnosis and underlying aetiology has also created difficulties in aetiological research. Without clear mechanistic hypotheses, the generation of appropriate disease models and development of targeted treatments are made very difficult."

PRISM has collected large phenotypic datasets to better understand the pathophysiological relationships underlying biologically-meaningful patient subgroups. The consortium notably conducted a preliminary clustering analysis of behavioural profiles, using passively collected smartphone app data. The latter revealed three distinct social profiles, but surprisingly, each of these profiles included healthy controls as well as schizophrenia and Alzheimer's disease patients. There was some overlap between patient groups.

"These new clusters clearly do not equate to existing diagnostic-based categorisation of patients. Ongoing studies are now adding in additional detail (e.g. neuro-imaging) from other components of the study. This emerging quantitative framework will both offer new ways to classify individuals and also offer insights into the biological mechanisms underlying these profiles," says Dr Marston, PRISM's second co-project coordinator on behalf of Eli Lilly and Company.

Next steps for PRISM

The PRISM consortium will keep analysing their datasets over the coming months, as well as collect new data with two future research activities in mind: replicating their initial clinical findings on new patient cohorts, and investigating the neurobiological mechanisms underlying these patient clusters.

The main difficulty in the construction of such biologically-valid diagnoses is the lack of objective biomarkers.

Drs Kas and Marston are hopeful that PRISM's novel approach will contribute to the acceleration of new treatment development, with improved efficacy and new mechanisms with more accurate assignment to the optimal patient. "We aim to facilitate improved solutions to the growing public health challenges of psychiatry and neurology," they conclude.

PROJECT
PRISM – Psychiatric Ratings using Intermediate Stratified Markers

COORDINATED BY
University of Groningen in the Netherlands

FUNDED UNDER
H2020-HEALTH-IMI2

CORDIS FACTSHEET
cordis.europa.eu/project/id/115916

PROJECT WEBSITE
prism-project.eu

Novel algorithms can predict psychosis before it strikes

Currently, the accurate prediction of psychoses relies on clinicians' best guess and experience. That may be about to change thanks to prediction algorithms developed under the PRONIA project.

Society's quest for ever more wealth, comfort and growth is driving citizens into a corner. Affective and non-affective psychoses have never been so widespread, to the point where they've become the most expensive brain-related disorder in Europe. In affective disorders, the pattern is often the same: a sedentary, sunlight-deficient, sleep-deprived lifestyle starting from a young age, combined with an increased use of drugs and growing emotional neglect.

"The cost for society is overwhelming," says Prof. Dr Nikolaos Koutsouleris from Ludwig-Maximilians University of Munich. "Younger populations are strongly affected, and the resulting disability over their lifetime – due to the frequently relapsing course of these disorders – causes very high direct and indirect costs in 50 % of cases." In Europe alone, psychotic and affective disorders amount to a burden of EUR 207 billion every year.

One might wonder how to rein in the rising tide of mental illness. According to Prof. Dr Koutsouleris, we're looking at three main breaches in current countermeasures. The first is that, in most EU countries, preventive psychiatry is still in its infancy, with no suitable mental healthcare infrastructures in place. The second reason lies in how early recognition strategies are derived from group-level statistical analyses, making it very difficult to reliably identify individuals at risk. Finally, early intervention procedures (mainly psychotherapy) are also derived from group-level clinical trials which have not been tailored to produce treatment recommendations for individual patients. People at high risk are very difficult to recruit for these clinical trials.

PRONIA's prognosis tools are tailored to populations highly at risk, where this risk has already been established by a clinician.

The PRONIA (Personalised Prognostic Tools for Early Psychosis Management) project was built around this need for more representative studies and personalisation tools. "In PRONIA, we aimed to address the second shortcoming, that is, the need for tools that allow for a more accurate and representative measurement of risk in the single patient. We also tried to operationalise poor outcomes more broadly by including the likes of functional impairment in our prediction target, as well as to include more objective data in our prognostic tools such as neuroimaging, neurocognitive data and genetic or proteomic information."

PRONIA's prognosis tools are tailored to high-risk populations, where this risk has already been established by a clinician. They complement the 'gut feeling' that currently rules patient prognosis with a quantification of the actual risk.

"In the future, this could lead to a stratified preventive approach and a more rational allocation of therapeutic resources. The main innovation resides in how we trained machine learning algorithms to predict outcomes at single-subject level, by feeding them with sequentially-acquired multi-modal prognostic data," Prof. Dr Koutsouleris explains. "In a sense, this mimics prognostic chains in real-world clinical settings. We add computer-aided support to these workflows to enhance medical decision-making at critical junctures in the process."

Concretely, clinical experts will be able to use a tool provided with quantitative risk estimates – risk scores – across different domains, such as risk for disease transition or risk for functional impairment at six-month, one-year or two-year follow-up points. Such an approach could facilitate a more flexible, broader and more accurate quantification of risk in each patient, although it does not resolve infrastructural challenges.

The PRONIA consortium is in the process of drafting a business plan for a company that will test the prototype telepsychiatric decision support system in real-world clinical environments across different EU countries. "Obviously, when moving from bench to bedside many challenges will have to be addressed, including certification, patient safety and ethical considerations," Prof. Dr Koutsouleris concludes.

PROJECT
PRONIA – Personalised Prognostic Tools for Early Psychosis Management

COORDINATED BY
Ludwig-Maximilians University of Munich in Germany

FUNDED UNDER
FP7-HEALTH

CORDIS FACTSHEET
cordis.europa.eu/project/id/602152

PROJECT WEBSITE
www.pronia.eu/

Night-time seizure detector improves quality of life for epileptic patients and carers

A new epileptic seizure detector pioneered by the EU-funded SEIZSAFE project gives privacy and security to patients and caregivers alike.

Around 50 million people around the world have epilepsy, 6 million living in Europe. Globally, an estimated 2.4 million are diagnosed each year. Epilepsy is characterised by recurrent seizures that carry the risk of injury, heart attack, brain damage and even death.

Around 20% of epileptic patients have seizures during the night. Caregivers, usually patients' relatives, reduce the risk of harm by staying alert all night and trying to mitigate the seizures, by holding the patients, putting them in a certain position or giving them medication.

"Many parents sleep with their epileptic child during the night to assist them when a seizure happens," says Diego Polo, SEIZSAFE (Patient-self-adaptive system for detection, recording and alert to caregivers of night-time seizures, linked to private cloud platform for patient tracking and big data exploitation) Project Manager at Encore Lab. "This is because the only way to be alerted is by being in a light sleep able to feel the child's movements. The consequences for caregivers are insomnia, sleep disorders and a potential lack of intimacy, the last consequence also experienced by the patient as they grow older," he says.

Night's Watch

The SEIZSAFE project sought to improve the quality of life of both patients and carers, by developing and marketing an effective and unobtrusive device to monitor patients and alert caregivers during night-time seizures when necessary. A detection system and motion sensors monitor all patient movement in real-time. An integrated algorithm automatically picks up seizures. Caregivers are alerted through a connected app, and a camera immediately starts filming the seizure activity.

The consequences for caregivers are insomnia, sleep disorders and a potential lack of intimacy, the last consequence experienced by the patient too as they grow older.

Caregivers can rest peacefully knowing that they will be alerted by the system should a seizure take place. This leads to higher levels of care and increased patient safety, while improving the quality of life of the carer. What's more, both patient and carer can have more privacy and personal space, as they are now able to sleep in separate rooms.

The system also provides doctors with a high-quality monitoring tool for diagnosis and treatment programmes, which can be tailored to each individual patient. Encrypted data is uploaded to a cloud, giving a complete historical record of seizure activity. Patients can decide if they want their anonymised information to be shared with the medical community to be used in future research.

"In the long term, it's possible to collect valuable data about the effectiveness of treatments and medication," says Polo. "We are not doctors and cannot help to cure epilepsy, but at least we are helping the families of patients to live better and also help towards finding a cure through contributing data."

Expanding the market

Some technical issues arose during the project but solutions were found by the team. "One big issue was a lack of data to test the algorithm and perform functioning tests. To resolve this, Encore contacted many patient associations looking for volunteers to help us to develop the device."

The device has already been tested in homes and hospitals and has a high detection accuracy. SeizSafe is expected to be launched in July 2019, and the team plans to expand its use into the European market. There are 1.2 million epilepsy patients suffering night-time seizures in Europe, and Encore foresees the uptake of 6.5 % of the market in five years: around 80 000 users, by the end of 2022.

PROJECT
SEIZSAFE – Patient-self-adaptive system for detection, recording and alert to caregivers of night-time seizures, linked to private cloud platform for patient tracking and big data exploitation

COORDINATED BY
Encore Lab in Spain

FUNDED UNDER
H2020-HEALTH, H2020-LEIT-ICT and H2020-SME

CORDIS FACTSHEET
cordis.europa.eu/project/id/726947

PROJECT WEBSITE
seizsafe.com/en

CORDIS Results Pack

Available online in six language versions: cordis.europa.eu/article/id/401587

Published
on behalf of the European Commission by CORDIS at the
Publications Office of the European Union
2, rue Mercier
L-2985 Luxembourg
LUXEMBOURG

cordis@publications.europa.eu

Editorial coordination
Zsófia TÓTH, Silvia FEKETOVÁ

Disclaimer
Online project information and links published in the current issue of the CORDIS Results Pack are correct when the publication goes to press. The Publications Office cannot be held responsible for information which is out of date or websites that are no longer live. Neither the Publications Office nor any person acting on its behalf is responsible for the use that may be made of the information contained in this publication or for any errors that may remain in the texts, despite the care taken in preparing them.

The technologies presented in this publication may be covered by intellectual property rights.

This Results Pack is a collaboration between CORDIS and the Innovative Medicines Initiative, the Directorate-General for Research and Innovation, the Directorate-General for Communications Networks, Content and Technology, and the European Research Council.

PRINT	ISBN 978-92-78-41981-3	ISSN 2599-8285	doi:10.2830/214233	ZZ-AK-19-011-EN-C
HTML	ISBN 978-92-78-41979-0	ISSN 2599-8293	doi:10.2830/017902	ZZ-AK-19-011-EN-Q
PDF	ISBN 978-92-78-41980-6	ISSN 2599-8293	doi:10.2830/24061	ZZ-AK-19-011-EN-N

Luxembourg: Publications Office of the European Union, 2019

RESEARCH*EU MAGAZINE ISSUE 83
Increasingly smart, increasingly sustainable: Europe's cities get an upgrade

Europe's cities are getting a smart and sustainable makeover. In this issue of Research*eu magazine, we feature seven EU-funded projects that are turning the notion of a 'digital city' from concept to reality, with a particular focus on smarter and more efficient mobility, waste management, air quality and citizen engagement.

Research*eu is free of charge.
Browse, download or subscribe at:
cordis.europa.eu/research-eu

Follow us on social media too!
facebook.com/EULawandPublications
twitter.com/CORDIS_EU
youtube.com/CORDISdotEU
instagram.com/cordis_eu

Publications Office of the European Union

EN